In the Claims

Please enter the following rewritten claims:

1. (Currently amended) A method of detecting an activity in a cell, comprising;

1) providing a cell comprising,

a) at least one destabilization domain, wherein said destabilization domain is non-cleavable by α-NH-ubiquitin protein endoproteases,

b) a reporter moiety, and

c) a linker moiety that operatively couples said destabilization domain to said reporter moiety,

wherein said linker moiety comprises a recognition motif for said activity and modification of said linker moiety by said activity modulates the coupling of said destabilization domain to said reporter moiety thereby modulating the stability of said reporter moiety, and

wherein said linker moiety is non-cleavable by said α-NH-ubiquitin protein endoproteases, and wherein the destabilization domain, the target protein, and the linker are encoded by one or more nucleic acid molecules in the cell,

2) detecting said reporter moiety, or a product of said reporter moiety, thereby detecting the activity in the cell.

2. (Currently amended) The method of claim 1, wherein said at least one destabilization domain is arranged as a linear multimer, and

wherein said linear multimer comprises at least two copies of said destabilization domain and is non-cleavable by said α-NH-ubiquitin protein endoproteases.

3. (Currently amended) The method of claim 1, wherein said linker moiety is a non-naturally occurring polypeptide or protein.

4. (Currently amended) The method of claim 1, wherein said linker moiety covalently couples said destabilization domain to said reporter [protein] moiety.

5. (Original) The method of claim 1, wherein said linker moiety is between about 1 and 30 amino acid residues.

6. (Original) The method of claim 1, wherein said destabilization domain comprises a ubiquitin homolog.

7. (Original) The method of claim 6, wherein said ubiquitin homolog comprises a mutation that prevents cleavage by said α-NH-ubiquitin protein endoproteases.

8. (Original) The method of claim 6, wherein said ubiquitin homolog comprises a mutation at glycine 76.

9. (Original) The method of claim 1, wherein said linker moiety comprises a first amino acid sequence that is covalently coupled to said reporter moiety, and a second amino acid sequence that is covalently coupled to said at least one destabilization domain.

10. (Original) The method of claim 1, wherein said activity is selected from the group consisting of a protease activity, a protein kinase activity and a phosphoprotein phosphatase activity.

11. (Original) The method of claim 1, wherein said reporter moiety is selected from the group consisting of a naturally fluorescent protein homolog, a β-lactamase homolog, a α-

galactosidase homolog, an alkaline phosphatase homolog, a CAT homolog, and a luciferase homolog.

12. (Original) The method of claim 11, wherein said reporter moiety comprises a β-lactamase homolog.

13. (Original) The method of claim 11, wherein said reporter moiety comprises an *Aequorea* Green fluorescent protein homolog.

14. (Original) The method of claim 11, wherein said reporter moiety comprises an Anthozoan Green fluorescent protein homolog.

15. (Original) The method of claim 1, wherein said cell is a mammalian cell.

16. (Original) The method of claim 1, wherein said cell is a yeast cell.

17. (Original) The method of claim 1, wherein said cell is an insect cell.

18. (Original) The method of claim 1, wherein said cell is a plant cell.

19. (Original) The method of claim 1, wherein said method further comprises the step of adding a protein synthesis inhibitor to said cell.

20. (Original) The method of claim 1, wherein said method further comprises the step of adding an inhibitor of said reporter moiety to said cell.

21. (Original) The method of claim 1, wherein said method further comprises the step of adding a test chemical to said cell.

22. (Previously amended) The method of claim 21, wherein said method further comprises the step of relating said reporter moiety activity before addition of said test chemical to said reporter moiety activity after addition of said test chemical.

23. (Currently amended) A method of regulating the concentration of one or more target proteins in a cell, comprising;

1) providing a cell comprising,

a) a linear multimerized destabilization domain, wherein said linear multimerized destabilization domain is non-cleavable by a α-NH-ubiquitin protein endoproteases, and comprises at least two copies of a destabilization domain,

b) a target protein, and

c) a linker that operatively couples said linear multimerized destabilization domain to said target protein,

wherein said linker comprises a protease cleavage site for a protease and cleavage of said linker by said protease modulates the coupling of said linear multimerized destabilization domain to said target protein, and wherein the destabilization domain, the target protein, and the linker are encoded by one or more nucleic acid molecules in the cell, thereby modulating the stability of said target protein in said cell, and

wherein said linker is non-cleavable by a α-NH-ubiquitin protein endoproteases,

2) providing said protease to cause cleavage of said linker thereby increasing the stability and concentration of said protein of interest in said cell.

24. (Original) The method of claim 23, wherein said protease is naturally expressed in said cell.

25. (Original) The method of claim 23, wherein said protease is not naturally expressed in said cell.

26. (Original) The method of claim 23, further comprising the step of adding an inhibitor of said protease.

27. (Original) The method of claim 23, wherein said linker is between 1 and 30 amino acid residues.

28. (Original) The method of claim 23, wherein said cell is a mammalian cell.

29. (Original) The method of claim 23, wherein said cell is a yeast cell.

30. (Original) The method of claim 23, wherein said cell is an insect cell.

31. (Original) The method of claim 23, wherein said destabilization domain comprises a ubiquitin homolog.

32. (Original) The method of claim 31, wherein said ubiquitin homolog comprises a mutation that prevents cleavage by α-NH-ubiquitin protein endoproteases.

33. (Original) The method of claim 31, wherein said ubiquitin homolog comprises a mutation at glycine 76.

34. (Original) The method of claim 23, wherein said protease is provided by transfecting said cell with an expression vector comprising a nucleic acid sequence encoding said protease.

35. (Original) The method of claim 34, wherein said expression vector further comprises an inducible promoter.

36. (Original) The method of claim 34, wherein said expression vector is a retroviral expression vector.

37. (Original) The method of claim 34, wherein said protease is a viral protease.

38. (Currently amended) A method of destabilizing a target protein in a cell, comprising;

A. introducing into the cell, one or more nucleic acid molecules that together encode a target protein and a linear multimerized destabilization domain, [operatively coupling a] wherein the target protein is operatively coupled to a linear multimerized destabilization domain, wherein said linear multimerized destabilization domain is non-cleavable by a α-NH-ubiquitin protein endoproteases, and comprises at least two copies of a destabilization domain, and wherein said destabilization domain comprises a ubiquitin homolog; and

B. allowing the target protein to be recognized by one or more elements of a cellular protein degradation apparatus, thereby destabilizing the target protein.

39. Cancelled

40. (Previously amended) The method of claim 38, wherein said ubiquitin homolog comprises a mutation that prevents cleavage by α-NH-ubiquitin protein endoproteases.

41-49 (Cancelled)

50. (Currently amended) A recombinant DNA molecule, comprising a nucleic acid sequence encoding;

a) a linear multimerized destabilization domain, wherein said linear multimerized destabilization domain is non-cleavable by [a] α-NH-ubiquitin protein endoproteases, and comprises at least two copies of a destabilization domain,

b) a target protein, and

c) a linker moiety that operatively couples said multimerized destabilization domain to said reporter moiety,

wherein said linker is non-cleavable by a α-NH-ubiquitin protein endoproteases.

51-54 (Cancelled)

55. (Currently amended) A recombinant protein molecule, comprising an amino acid sequence encoding for;

a) a linear multimerized destabilization domain, wherein said multimerized destabilization domain is non-cleavable by [a] α-NH-ubiquitin protein endoproteases, and comprises at least two copies of said destabilization domain,

b) a target protein, and

c) a linker moiety that operatively couples said multimerized destabilization domain to said reporter moiety,

wherein said linker is non-cleavable by a α-NH-ubiquitin protein endoproteases.

56-59 (Cancelled)

60. (Currently amended) A host cell, comprising a nucleic acid sequence encoding [for];

a) a linear multimerized destabilization domain, wherein said multimerized destabilization domain is non-cleavable by a α-NH-ubiquitin protein endoproteases, and comprises at least two copies of said destabilization domain,

b) a target protein, and

c) a linker moiety that operatively couples said multimerized destabilization domain to said reporter moiety,

wherein said linker is non-cleavable by a -NH-ubiquitin protein endoproteases.

61-79 (Cancelled)

80. (Previously added) The method of claim 1, wherein the method is performed *in vitro*.

81. (Previously added) The method of claim 23, wherein the method is performed *in vitro*.

82. (Previously added) The method of claim 38, wherein the method is performed *in vitro*.

Please add the following claims:

--83. (New) The method of claim 1, wherein the cell is from an organism other than a transgenic organism.

84. (New) The method of claim 38, wherein the cell is from an organism other than a transgenic organism.

85. (New) The method of claim 1, wherein the cell is from a transgenic rodent.

86. (New) The method of claim 1, wherein the cell is from a transgenic plant.--